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Effect of acute noxious stimulation to the leg or back on muscle synergies during walking

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van den Hoorn W, Hodges PW, van Dieën JH, Hug F. Effect of acute noxious stimulation to the leg or back on muscle synergies during walking. *J Neurophysiol* 113: 244–254, 2015. First published October 8, 2014; doi:10.1152/jn.00557.2014.—This study aimed to examine how acute muscle pain affects muscle coordination during gait with consideration of muscle synergies (i.e., group of muscles activated in synchrony), amplitude of muscle activity and kinematics. A secondary aim was to determine whether any adaptation was specific to pain location. Sixteen participants walked on a treadmill during 5 conditions [control, low back pain (LBP), washout LBP, calf pain (CalfP), and washout CalfP]. Five muscle synergies were identified for all of the conditions. Cross-validation analysis showed that muscle synergy vectors extracted for the control condition accounted for >81% of variance accounted for from the other conditions. Muscle synergies were altered very little in some participants ($n = 7$ for LBP; $n = 10$ for CalfP), but were more affected in the others ($n = 9$ for LBP; $n = 6$ for CalfP). No systematic differences between pain locations were observed. Considering all participants, synergies related to propulsion and weight acceptance were largely unaffected by pain, whereas synergies related to other functions (trunk control and leg deceleration) were more affected. Gastrocnemii activity was less during both CalfP and LBP than control. Soleus activity was further reduced during CalfP, and this was associated with reduced plantar flexion. Some lower leg muscles exhibited adaptations depending on pain location (e.g., greater vastus lateralis and rectus femoris activity during CalfP than LBP). Overall, these changes in muscle coordination involve a participant-specific strategy that is important to further explore, as it may explain why some people are more likely to develop persistence of a painful condition.

motor modules; experimental pain; muscle coordination; gait; non-negative matrix factorization

PAIN ALTERS MOTOR CONTROL. For instance, motor drive is redistributed within and between muscles during experimental pain. This is reflected by reduced drive to some motor units in the painful muscle (Farina et al. 2004) and its synergists (Hodges et al. 2008) and increased drive to others to maintain force output (Bank et al. 2013; Hodges and Tucker 2011; Murray and Peck 2007; Tucker and Hodges 2010). These adaptations have been extensively documented during single-joint isometric tasks that provide few options for the central nervous system (CNS) to vary the manner in which a task is performed.

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Less is known for walking, which involves multiple degrees of freedom, and thus various possibilities for adaptation in muscle coordination while maintaining the overall demands of locomotion.

During walking, the CNS controls numerous muscles, which simultaneously contribute to multiple functions (e.g., propulsion, posture, balance, breathing), with considerable redundancy. Muscle synergies (motor modules) involve multiple muscles activated in synchrony. They have been proposed as building blocks activated by a single neural command to simplify the control of these numerous degrees of freedom (Cappellini et al. 2006; Ivanenko et al. 2004; Neptune et al. 2009; Ting and McKay 2007). Five discrete muscle synergies have been identified during gait (Cappellini et al. 2006; Ivanenko et al. 2004; Monaco et al. 2010; Oliveira et al. 2014). As muscle synergies are associated with functional subtasks of the gait cycle (Chvatal and Ting 2012; Ivanenko et al. 2006), the number of synergies provides information about the complexity of control (Clark et al. 2010), whereas changes in the composition/activation of synergies can indicate whether and how the control of these motor subtasks is altered (Safavynia et al. 2011). Investigation of muscle synergies provides an ideal method to probe the effect of pain on neural control strategies during multisegmental tasks such as walking.

Simple measures of temporal and spatial features of muscle activation recorded with electromyography (EMG) have revealed changes during gait when challenged by acute experimental pain. Some studies report a change in magnitude of activation and/or shape of myoelectric patterns in a small subset of muscles in the vicinity of the pain site (Arendt-Nielsen et al. 1996; Henriksen et al. 2007; Lamothe et al. 2004). However, it is unclear whether these adaptations arise from a generalized change in muscle synergies and therefore locomotor strategy. Reorganization of muscle synergies with acute pain has been reported during a reaching task in some but not all participants (Muceli et al. 2014). Although no pain-related changes in the synergy related to coupling between the elbow and shoulder joints were observed, other synergies were affected (Muceli et al. 2014). Similar adaptation might occur during walking, i.e., the synergies related to power production (propulsion and weight acceptance; Allen and Neptune 2012) might undergo little/no adaptation with pain, whereas synergies associated with postural subtasks could be more affected but with participant-specific strategies (Hodges et al. 2013; Muceli et al. 2014). A better understanding of how pain

impacts movement can be gained by investigation of this hypothesis related to modular control of walking, and furthermore, whether the location of pain differentially affects these adaptations.

We aimed to study the effect of experimental muscle pain on muscle coordination (as reflected by muscle synergies and amplitude of muscle activity) and kinematics during treadmill walking. In addition, we compared two pain locations: one in a muscle responsible for propulsion (medial gastrocnemius), and another in a muscle indirectly involved in gait (erector spinae). We hypothesized that muscle synergies related to power production (propulsion and weight acceptance; Allen and Neptune 2012) would remain unaltered by pain, regardless of its location. We further hypothesized that muscle synergies related to trunk control would exhibit more changes, but that this could involve a participant-specific strategy given recent work highlighting interindividual variability in pain adaptations (Hodges et al. 2013; Muceli et al. 2014).

MATERIAL AND METHODS

Participants

Seventeen healthy volunteers (6 women) participated in this experiment (age: 21 ± 2 yr, weight: 66 ± 11 kg, height: 173 ± 10 cm). Participants had no history of back or lower limb pain that had limited function or required them to seek intervention from a health care professional. Participants provided written, informed consent. The Institutional Medical Research Ethics Committee approved the study, and all of the procedures conformed to the Declaration of Helsinki. One participant (#2) fainted during positioning of surface EMG electrodes. Thus data are reported for 16 participants.

Experimental Setup

Experiments were conducted on a motor-driven treadmill (BH fitness, Pioneer pro) at 0.94 ms^{-1} and at 1.76 ms^{-1} (the higher speed was recorded for a separate experiment). Motion data were collected using an eight-camera movement recording system (T040, Vicon Motion Systems, Oxford, UK). Cameras were placed around the treadmill at a height of 2.8 m and at a distance between 2 and 6 m. Reflective markers (diameter: 14 mm) were attached to the skin with double-sided tape according to the Vicon Plug-in-Gait marker set (forearm and hand segments were excluded from the model). Movement data were sampled at 100 samples/s.

Myoelectric activity was recorded from a total of 19 muscles on the right side of the body. Surface electrodes were used for 15 muscles: tibialis anterior (TA), soleus (SOL), gastrocnemius medialis (GM) and lateralis (GL), vastus medialis (VM) and lateralis (VL), rectus femoris (RF), long head of biceps femoris (BF), semimembranosus (SM), gracilis (GRA), gluteus maximus (GMX) and medius (GMD), tensor fasciae latae (TFL), erector spinae at the level of the L_3 spinous process (ES), and rectus abdominis (RA). An additional channel was used to record electrocardiogram (ECG) to aid its removal from EMG recordings. Pairs of surface Ag/AgCl electrodes (Blue sensor, N-00-S, Ambu) were attached to the skin (~ 2 cm interelectrode distance). Electrodes were placed longitudinally with respect to the muscle fiber alignment at sites recommended by SENIAM when available (Hermens et al. 2000). Skin was shaved and cleaned with alcohol to reduce impedance. Electrode cables were well secured to the skin with adhesive tape, to minimize movement artifacts. EMG signals were amplified $\times 1,000$, band-pass filtered (bandwidth 10–1,000 Hz), and digitized with 22-bit precision at 2,048 samples/s (PortiLab 2, TMS International).

Intramuscular EMG electrodes were used to record myoelectric activity from the four other muscles: obliquus internus (OI) and

externus (OE) abdominis, iliocostalis at the level of the L_3 spinous process (IL), and longissimus at the level of T_{12} spinous process (LO). Fine-wire EMG electrodes [two Teflon-coated 100- μm stainless-steel wires with 2-mm insulation removed, bent back at 2 and 4 mm to form hooks, and threaded into a hypodermic needle ($22 \text{ G} \times 38 \text{ mm}$ or $22 \text{ G} \times 70 \text{ mm}$, depending on the muscle depth)] were inserted with ultrasound guidance (12 MHz, Logic E, GE Healthcare). Skin was cleaned with antiseptic. Note that no participants reported pain at the location of the fine-wire insertion during the experiment. Intramuscular EMG data were preamplified $\times 2,000$, band-pass filtered (10–1,000 Hz for subjects 1–8: Telemyo, Noraxon; 30–1,000 Hz for subject 9–17: Neurolog, Digitimer) and digitized with 16-bit precision with a Power1401 Data Acquisition System with Spike2 software (Cambridge Electronic Design) at 2,000 samples/s. EMG and movement data were synchronized with a transistor-transistor logic pulse at the beginning and end of each condition.

Procedure

Participants were familiarized with treadmill walking for 1–5 min before the start of the experiment. Walking trials of 6-min duration were repeated in five experimental conditions: control; low back pain (LBP); washout LBP; calf pain (CalfP); and washout CalfP. The 6-min trials included 3 min of walking at 0.94 ms^{-1} and 3 min at 1.76 ms^{-1} in random order. For the purpose of this study, only the lowest speed was analyzed (0.94 ms^{-1}). All participants began with the control condition that was considered the reference for both pain conditions. The order of pain induction into either the low back or calf was also randomized. Participants rested in sitting between conditions. Each “washout” condition began ~ 4 min after full recovery of pain.

Experimental pain. Muscle pain was induced by injection of a single bolus of hypertonic saline into the right ES muscle adjacent to the L_3 spinous process or the right GM muscle [for both muscles: 0.7 ml, 7% NaCl (Hug et al. 2014a)]. To account for the decrease in pain intensity after ~ 2 –3 min, a second injection was administered before the start of the second speed. Pain intensity was reported verbally every 30 s during the painful conditions on an 11-point numerical rating scale, anchored with “no pain” at 0 and “worst pain imaginable” at 10 (Tucker et al. 2014). During the pain trial, recording began after the pain intensity reached 2/10 and stopped when pain intensity dropped below 2/10 (Hug et al. 2014b; Tucker and Hodges 2010). Participants recorded the area of pain on a standardized diagram of the leg and back following each pain trial (Fig. 1).

Data Analysis

Kinematics of walking. Fifteen complete stride cycles (consecutive heel strikes on the right side) were selected for analysis based on quality of the EMG data (see *EMG preprocessing*). Heel strikes were determined from the local vertical minima of the right heel marker position. Toe offs were determined from the local maximum of the vertical velocity of the right heel marker. Stride time (complete gait cycle) was the time between consecutive heel strikes of the right leg, stance time was the time between heel strike and the consecutive toe off, and swing time was the time between toe off and the consecutive heel strike.

The plug-in-gait model was used to calculate the spine angles (angle between pelvis and thorax) in the horizontal (rotation), frontal (lateral-flexion) and sagittal (flexion-extension) planes. Hip, knee and ankle angles were calculated in the sagittal plane (flexion-extension) on both sides. The minimum/maximum range of motion (ROM) and total ROM were determined within each stride cycle and averaged across the 15 stride cycles.

EMG preprocessing. EMG signals were band-pass filtered (20–750 Hz for surface EMG and 50–750 Hz for intramuscular EMG) with a zero-lag fourth-order Butterworth filter. Based on visual inspection, a

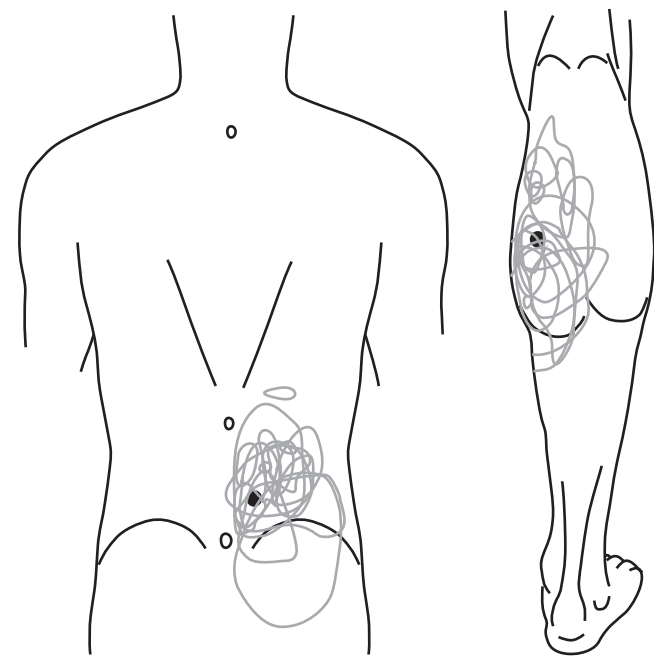


Fig. 1. Area of pain. Pain location was reported by each participant when hypertonic saline was injected (at the sites indicated by the black dot) into the right erector spinae muscle at the level of the L₃ spinous process and the right medial gastrocnemius muscle.

section of EMG data containing at least 15 consecutive stride cycles without artifacts (e.g., movement) was selected for analysis. RA and GRA EMG were discarded for all participants, because EMG amplitude was consistently very low, artifacts were found in most cases, and signals appeared contaminated by cross talk from adjacent muscles. If 15 consecutive cycles were not available without artifacts, recording for that muscle was discarded from further analysis for that participant. Table 1 depicts muscles available for analysis for each participant.

ECG artifacts were removed from the ES, GMX and GMD EMG recordings. Each QRS complex was detected from the ECG signal (Mulder 1992). From the unfiltered EMG signal, a 12-ms window (± 6 ms) was extracted around the time of detected heartbeats, to create an ensemble average of the representative ECG artifacts in a muscle. The

template created from this average was subtracted from the EMG signal at the ECG time points before filtering.

EMG data were rectified and subsequently smoothed with a 9-Hz, fourth-order zero-lag low-pass Butterworth filter (Shiavi et al. 1998). For both synergy and EMG amplitude analysis, EMG data were normalized to the average of the peak values across the 15 cycles of the control condition. EMG amplitude was calculated as the average of the mean normalized EMG amplitudes recorded during each of the 15 stride cycles.

Extraction of muscle synergies for each condition independently. As intercycle variability contains important information for identification of muscle synergies (Clark et al. 2010), they were extracted using nonnegative matrix factorization (Lee and Seung 2001, 1999) from a set of 15 consecutive cycles, as previously described by Hug et al. (2011) and Frere and Hug (2012). The decomposition algorithm has two components: the “muscle synergy vectors” that represent the relative weighting of each muscle within each synergy and the “synergy activation coefficients” that represent the recruitment of the muscle synergy across the gait cycle (for details, see Ting and Chvatal 2010). The algorithm is based on iterative updates of an initial random guess of muscle synergy vectors and synergy activation coefficients that converge to a local optimal matrix factorization (for details, see Lee and Seung 2001). The algorithm was repeated 20 times for each participant in each condition. The lowest cost solution was retained (i.e., minimized squared error between original and reconstructed EMG patterns).

The initial EMG matrix consisted of 15 consecutive cycles for all the muscles. Each cycle was interpolated to 200 time points. The EMG matrix was thus a 15- to 17-row (depending on the number of retained muscles, Table 1) and 3,000-column matrix. Mean total variance accounted for (VAF) was calculated (Frere and Hug 2012; Torres-Oviedo et al. 2006). For each participant’s data, the analysis was iterated by varying the number of synergies between 1 and 15, and then the lowest number of synergies that accounted for more than 90% of the variance (Torres-Oviedo and Ting 2007), while adding an additional synergy did not increase VAF by more than 3%, was selected. Data from all participants and the five experimental conditions (80 trials) revealed two, three, four, five and six muscle synergies in 1, 2, 24, 58 and 15% of cases, respectively. For each participant and each condition the same number of muscle synergies (i.e., 5) were extracted to facilitate comparison of the set of synergies (Roh et al. 2012) between conditions/participants. This choice was further motivated by the fact that most previous studies identified five

Table 1. Muscles selected for synergy analysis in each participant

	Participants																
Muscles	1	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
TA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
SOL	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
GM	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
GL	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
VM	x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	
VL	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
RF	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
BF	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
SM	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
GMX	x		x	x	x	x	x	x		x	x	x	x	x	x	x	
GMD	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
TFL	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
ES	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	
OI	x	x	x	x	x	x	x		x		x	x		x	x	x	
OE							x	x		x		x		x			
IL	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	
LO	x	x	x	x	x	x		x	x	x	x	x	x	x	x	x	

“x” indicates that the muscle was selected for data analysis. For muscle name abbreviations, see MATERIALS AND METHODS.

muscle synergies during walking (Cappellini et al. 2006; Ivanenko et al. 2004; Monaco et al. 2010; Oliveira et al. 2014).

Cross-validation of the extracted muscle synergies. To verify the robustness of the extracted muscle synergies across conditions, we used a cross-validation procedure (Cheung et al. 2005, 2009; Clark et al. 2010; Hug et al. 2011; Torres-Oviedo and Ting 2007, 2010; Turpin et al. 2011). First, muscle synergy vectors extracted from the control condition (*control 1*) were used to reconstruct the individual EMG patterns of another set of 15 consecutive stride cycles within the same condition (*control 2*, separated by 162 ± 60 stride cycles). This first step allowed us to determine the within-subject variation of the synergies without pain. Second, muscle synergy vectors extracted from *control 1* were used to reconstruct the individual EMG patterns of all other conditions. To do this, the muscle synergy matrix extracted from the control condition (\mathbf{W}_{cont}) was held fixed in the algorithm, and the activation coefficients matrix ($\mathbf{C}_{\text{condition}}$) was free to vary. $\mathbf{C}_{\text{condition}}$ was initialized with random values and iteratively updated until convergence. The EMG data matrix ($\mathbf{E}_{\text{condition}}$) of the other conditions was provided to the algorithm with the following update rule (Lee and Seung 2001):

$$(\mathbf{C}_{\text{condition}})_{ij} \leftarrow (\mathbf{C}_{\text{condition}})_{ij} \frac{(\mathbf{W}_{\text{cont}}^T \mathbf{E}_{\text{condition}})_{ij}}{(\mathbf{W}_{\text{cont}}^T \mathbf{W}_{\text{cont}} \mathbf{C}_{\text{condition}})_{ij}} \quad (1)$$

In addition, to compare pain locations, the muscle synergy vectors of the LBP condition were used to reconstruct the EMG patterns of the CalfP condition. We considered that the synergies were significantly affected by pain (or by pain location) if the VAF was reduced by more than the upper limit of the 95% confidence interval of the VAF change when EMG patterns of *control 2* were reconstructed using synergy vectors of *control 1*.

Assessment of similarity between muscle synergies. The similarity between the muscle synergies extracted from the control condition and those extracted from each other condition was further determined by correlation analyses. Similarity in synergy activation coefficient and muscle synergy vectors between conditions was assessed using Pearson cross-correlation (r_{max}) and correlation (r) coefficients, respectively. They were considered similar when the coefficient was higher than 0.80 (Hug et al. 2010). In addition, to compare pain locations, the similarity between the LBP and CalfP conditions was also determined.

Statistical Analysis

Statistical analyses were performed in Stata (StataCorp) using a linear mixed model. Condition (control, LBP, washout LBP, CalfP, washout CalfP) was entered as a fixed effect, and the intercepts of the participants were entered as random effects into the model. P values were obtained via maximum likelihood. Significance level was set at $P \leq 0.05$.

If the Shapiro-Wilk test for normality was significant, data were transformed.

Pain intensities during the 15 analyzed stride cycles were compared between the LBP and CalfP conditions with a paired t -test. The linear mixed model assessed differences in the dependent variables (EMG amplitude of each muscle, VAF, cross-validated VAF) between the five conditions. If the main effect of condition was significant, then LBP, washout LBP, CalfP and washout CalfP conditions were compared with the control condition, and the two pain conditions were compared using a post hoc Wald test with Bonferroni correction for multiple comparisons (adjusted P values are reported). For the kinematics data, condition, side and the condition \times side interaction were added into the linear mixed model as fixed effects. If the condition \times side interaction was significant, the effect of condition was tested within each side, with Bonferroni correction for multiple comparisons (adjusted P values are reported).

Changes in EMG amplitude during LBP and CalfP conditions were also analyzed on an individual basis. For each participant and each

muscle, the EMG amplitude was defined conservatively as increased or decreased if its change exceeded 15% of that in the control condition (Hodges et al. 2013).

RESULTS

Pain Intensity

The average pain intensity during the 15 stride cycles was 5.3 ± 1.8 for LBP and 5.8 ± 1.7 for CalfP (t -test for LBP vs. CalfP; $P = 0.10$). Location of pain was restricted to the lumbar region for LBP and to the medial calf for CalfP and was primarily reported in the vicinity of the hypertonic saline injections (Fig. 1).

Kinematics of Walking

In both painful and nonpainful side, stride and stance times were less during LBP and CalfP than control (condition effect: both $P < 0.01$; post hoc: all $P < 0.01$), but there was no difference between the two pain conditions ($P = 0.07$ and $P = 0.08$ for stride and stance time, respectively; Fig. 2). Swing time on the nonpainful side was less during CalfP than control (condition \times side interaction: $P < 0.01$; post hoc: $P < 0.01$) but was not different between LBP and control ($P = 0.79$). These changes observed during CalfP mainly reflect the observation of limping.

Although CalfP affected ankle kinematics on the painful side, LBP had a bilateral effect on hip kinematics and some specific adaptations in trunk kinematics (Table 2). Plantar flexion was less during CalfP on the painful side than control (condition \times side interaction: $P = 0.05$; post hoc: $P < 0.01$), but no change was observed on the nonpainful side (all $P > 0.11$). No change in dorsiflexion was observed (condition effect: $P = 0.60$; condition \times side interaction: $P = 0.96$). Consequently, the ankle ROM was less during CalfP on the painful side than control (condition \times side interaction: $P = 0.03$; post hoc: $P < 0.01$). During the LBP condition, hip ROM

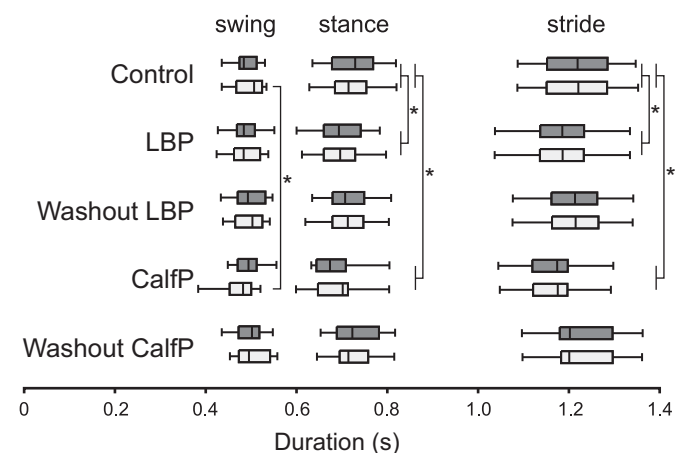


Fig. 2. Basic gait parameters. Swing time, stance time and stride time on the right (painful side, dark gray) and left (light gray) side are shown for the control, low back pain (LBP), washout low back pain (washout LBP), calf pain (CalfP) and washout calf pain (washout CalfP) conditions. During the LBP and CalfP conditions, hypertonic saline was injected into the erector spinae muscle at the level of the L₃ spinous process and medial gastrocnemius on the right side, respectively. Brackets with vertical lines indicate that both sides exhibited similar changes. *Significant ($P < 0.05$) differences between conditions. Error bars, 95% confidence interval (CI); box, 25th to 75th percentile with the median.

Table 2. Kinematics of ankle, knee, hip, and spine

	Control		LBP		Washout LBP		Calf Pain		Washout CalfP	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Ankle										
Plantar flexion	-22.9 (7.6)	-22.2 (7.9)	-19.2 (7.2)	-21.6 (7.6)	-21.3 (8.0)	-21.6 (7.9)	-15.7 (8.1)*	-21.0 (7.6)	-22.0 (7.8)	-22.7 (9.6)
Dorsal flexion	12.8 (4.2)	12.2 (6.1)	13.1 (4.4)	12.8 (5.9)	13.7 (4.4)	13.7 (5.9)	14.1 (5.0)	12.9 (5.9)	13.5 (4.8)	13.1 (6.7)
ROM	35.8 (9.9)	34.4 (6.6)	32.3 (6.5)	34.4 (8.0)	34.9 (7.7)	35.4 (8.0)	29.8 (6.7)*	33.9 (7.4)	35.5 (7.5)	35.8 (9.9)
Knee										
Extension	-2.5 (6.2)	-2.0 (4.8)	-1.4 (6.8)	-0.0 (5.8)	-2.6 (6.8)	-1.2 (5.8)	0.4 (7.7)	-1.1 (5.4)	-2.5 (6.5)	-1.6 (5.5)
Flexion	51.3 (8.2)	49.7 (9.5)	50.7 (7.3)	51.1 (8.3)	50.4 (8.4)	52.0 (7.7)	49.7 (9.0)	51.1 (7.6)	51.2 (7.5)	51.3 (8.5)
ROM	53.8 (3.6)	51.7 (6.6)	52.1 (5.0)*	51.1 (6.4)*	53.0 (4.9)	53.2 (5.7)	49.4 (7.9)	52.2 (6.2)	53.7 (4.7)	52.9 (6.5)
Hip										
Extension	-7.3 (6.9)	-8.2 (6.0)	-5.4 (7.9)	-6.6 (7.1)	-7.2 (7.5)	-7.8 (6.6)	-4.4 (6.8)	-8.1 (5.7)	-6.8 (7.8)	-7.7 (7.0)
Flexion	35.2 (7.7)	35.0 (7.2)	34.9 (8.0)	35.1 (8.2)	34.8 (7.9)	34.9 (7.8)	36.0 (7.3)	35.5 (7.4)	35.5 (7.8)	35.3 (8.3)
ROM	42.5 (3.8)	43.2 (5.1)	40.3 (4.1)	41.6 (5.1)	42.0 (4.0)	42.7 (5.0)	40.4 (4.3)	43.6 (5.8)	42.2 (3.7)	43.0 (5.3)
	Control		LBP		Washout LBP		Calf Pain		Washout CalfP	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
Spine flexion-extension										
Extension		-7.7 (9.8)		-5.6 (10.2)*		-7.0 (9.3)		-6.7 (10.3)		-7.5 (11.0)
Flexion		-3.7 (9.4)		-1.4 (9.7)*		-2.6 (9.2)		-1.8 (9.4)		-2.8 (10.1)
ROM		4.0 (1.2)		4.1 (1.7)		4.3 (1.5)		4.9 (2.6)*#		4.7 (1.9)
Spine rotation										
Left rotation		-5.7 (3.9)		-5.2 (3.4)		-5.6 (3.6)		-6.2 (3.7)		-5.3 (3.6)
Right rotation		5.3 (2.0)		4.6 (2.0)#		5.1 (1.9)		5.2 (2.5)		5.6 (2.3)
ROM		11.0 (4.2)		9.8 (3.3)*#		10.7 (3.2)		11.4 (4.8)		10.9 (3.4)
Spine lateral flexion										
Left lateral flexion		-3.3 (3.1)		-4.0 (2.8)		-4.0 (3.1)		-4.0 (3.2)		-4.0 (3.3)
Right lateral flexion		4.2 (2.7)		3.4 (3.0)*#		4.3 (3.0)		4.6 (2.9)		5.0 (3.9)
ROM		7.5 (3.8)		7.4 (3.9)		8.3 (3.9)		8.6 (4.1)		9.0 (4.4)

Values are means (SD) in degrees for hip, knee, ankle and spine minimum, maximum and range of motion (ROM) for the control, low back pain (LBP), washout LBP, calf pain (CalfP), and washout CalfP conditions. *Significant ($P < 0.05$) difference from control. #Significant difference between LBP and CalfP.

was less on both sides than control (condition effect: $P = 0.01$; post hoc: $P < 0.01$). However, there was no significant difference between the pain locations ($P = 1.00$). Knee kinematics was not affected (condition effect: all $P > 0.06$; condition \times side interactions: all $P > 0.13$).

During LBP, participants walked with a more flexed spine than the control condition; extension was less (main effect condition: $P < 0.01$; post hoc: $P < 0.01$) and flexion was greater (main effect condition: $P = 0.01$; post hoc: $P < 0.01$). There was no significant difference between the pain locations (both $P > 0.41$). Spine flexion/extension ROM was greater during CalfP than control and LBP (condition effect: $P = 0.03$; post hoc: both $P = 0.05$). Spine rotation ROM was less during the LBP than control and CalfP (condition effect: $P < 0.01$; post hoc: both $P < 0.01$). Spine rotation to the right (painful side) was also less during LBP than CalfP condition (condition effect: $P = 0.02$; post hoc: $P = 0.01$). However, spine rotation to the left was not affected by condition ($P = 0.26$). Lateral flexion to the painful side was less during LBP than both control and CalfP conditions (condition effect: $P < 0.01$; post hoc: both $P < 0.02$). Lateral flexion to the nonpainful side was not significantly affected by condition ($P = 0.06$).

EMG Amplitude

Although gastrocnemii muscle activity reduced during both pain conditions relative to control, there were some specific changes in EMG amplitude, depending on pain location, such as less SOL activity and greater VL and RF activity during CalfP than LBP (Figs. 3 and 4). A main effect of condition was observed in TA, SOL, GM, GL, VM, VL, RF, ES, IO and IL

(all $P < 0.01$). However, BF, SM, GMX, GMD, TFL, EO and LO were unaffected (all $P > 0.07$).

LBP was associated with reduced EMG amplitude of ankle plantar flexor muscles [GM ($P < 0.01$) and GL ($P = 0.05$)] than control, and this did not recover during washout LBP ($P < 0.01$ for GM and $P = 0.02$ for GL; Fig. 4). There was no significant systematic effect of pain on trunk muscle EMG amplitude when walking with LBP relative to control (all, $P > 0.62$). Although not different during LBP, EMG amplitudes of TA ($P = 0.02$) and ES ($P < 0.01$) were lower when walking during washout LBP (after recovery of LBP) than during control.

During CalfP, EMG amplitudes of the four lower leg muscles were lower than control (TA, SOL, GM, and GL; all $P < 0.01$), and amplitude for three did not recover during washout CalfP (SOL, GM: $P = 0.01$; GL: $P = 0.03$). In contrast, EMG amplitudes of knee extensor muscles (VM and VL) were higher (both $P = 0.05$) during CalfP than control. ES EMG amplitude was lower during washout CalfP than control ($P = 0.03$). During CalfP, SOL EMG amplitude was lower than during LBP ($P = 0.03$). RF EMG amplitude was higher during CalfP than LBP ($P = 0.01$).

Interindividual variability of changes in EMG amplitudes. Changes in EMG amplitude of some muscles varied between participants. Figure 5 shows the percentage of participants who exhibited decreased or increased EMG amplitude ($>15\%$) or no change for each muscle during the LBP and CalfP conditions relative to the amplitude recorded in the control condition. Qualitatively, the muscles that most commonly increased in EMG amplitude during LBP were OI (61.5%), then OE

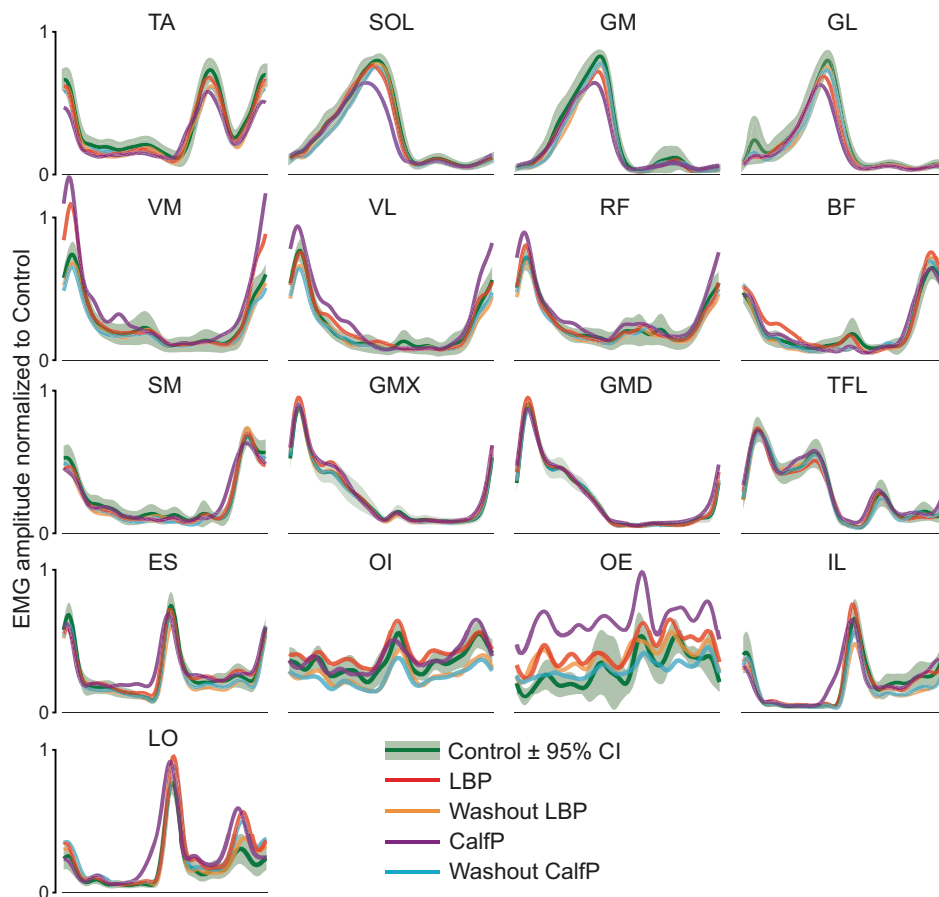


Fig. 3. Ensemble-averaged patterns of myoelectric activity. Patterns of myoelectric activity averaged across all participants are shown for control [green \pm 95% CI ($1.96 \times$ SEM)], LBP (red), washout LBP (orange), CalfP (purple) and washout CalfP (blue) conditions. Electromyographic (EMG) activity was normalized to the mean of the peaks within each stride cycle of the control condition. TA, tibialis anterior; SOL, soleus; GM, gastrocnemius medialis; GL, gastrocnemius lateralis; VM, vastus medialis; VL, vastus lateralis; RF, rectus femoris; BF, biceps femoris; SM, semimembranosus; GMX, gluteus maximus; GMD, gluteus medius; TFL, tensor fasciae latae; ES, erector spinae; OE, obliquus externus; IL, iliocostalis; LO, longissimus.

(42.9%) and LO (40%). It is important to note that activity of these muscles underwent an opposite change (i.e., a decrease) in 23.1, 28.6 and 33.3% of participants, respectively. During CalfP, EMG amplitude increased most commonly for OE (85.7%), RF (56.3%), VL (50%), and VM (43.8%). EMG commonly decreased for TA (68.8%), SOL (56.3%) and GM (37.5%), consistent with the average change in EMG amplitude.

Muscle Synergies Extracted for Each Condition Separately

Five muscle synergies were extracted for each participant during all conditions, and this accounted for a VAF of $90.8 \pm 1.4\%$, $93.3 \pm 1.4\%$, $92.2 \pm 1.8\%$, $93.3 \pm 1.8\%$, and $91.9 \pm 2.0\%$ for control, LBP, washout LBP, CalfP, and washout CalfP conditions, respectively. VAF differed between conditions (condition effect: $P < 0.01$). The VAF explained by five synergies was higher for the two pain conditions (LBP and CalfP vs. control, post hoc both: $P < 0.01$) and the two washout conditions (washout LBP, $P < 0.01$ and washout CalfP vs. control, post hoc: $P = 0.01$) than for the control condition.

Functional role of the extracted muscle synergies. The five identified muscle synergies (Fig. 6; Table 3) are similar to those reported previously for similar walking speeds (Cappellini et al. 2006; Ivanenko et al. 2004) and can be related to the subtasks of the gait cycle. *Synergy 1* ("propulsion" synergy) mainly involved the triceps surae muscles (GM, GL and SOL) and was active during the late stance. *Synergy 2* ("leg deceleration" synergy) mainly involved thigh muscles (SM, BF, VM

and VL) and was active during late swing/early stance phase. *Synergy 3* ("trunk flexion" synergy) mainly involved abdominal muscles (OI, OE) and TA and was active during swing and throughout the gait cycle. This synergy showed substantial interindividual variation in composition. *Synergy 4* ("trunk extension" synergy) involved the trunk extensors (IL, ES, LO) and was active during late stance. Finally, *synergy 5* ("weight acceptance" synergy) involved hip (GMX and GMD) and knee extensor (VL, VM and RF) muscles and was mainly active during early stance.

Cross-validation of muscle synergies. The cross-validation procedures showed that pain affected muscle synergies in some but not all participants. To assess the robustness of the muscle synergies across conditions, muscle synergy vectors extracted from *control 1* were used to reconstruct the EMG patterns in the other conditions. They explained more than 81% of the VAF in all conditions (average VAF across participants: $87.1 \pm 6.8\%$, $82.1 \pm 9.1\%$, $85.4 \pm 6.3\%$, $81.2 \pm 13.2\%$, and $84.9 \pm 8.9\%$ for the *control 2*, LBP, washout LBP, CalfP, and washout CalfP, respectively). There was a significant main effect of condition ($P < 0.01$). VAF values of both LBP ($P < 0.01$) and CalfP ($P < 0.01$) conditions were lower than those of *control 2*. This means that, on average, muscle synergy vectors were altered by experimental pain. As shown in Fig. 7, the change in VAF varied between participants during pain.

To investigate the individual adaptations, we calculated the upper limit of the 95% confidence interval of the change in VAF between *control 1* and *control 2*. Considering this threshold (-6.1%), muscle synergies were not affected by any of the

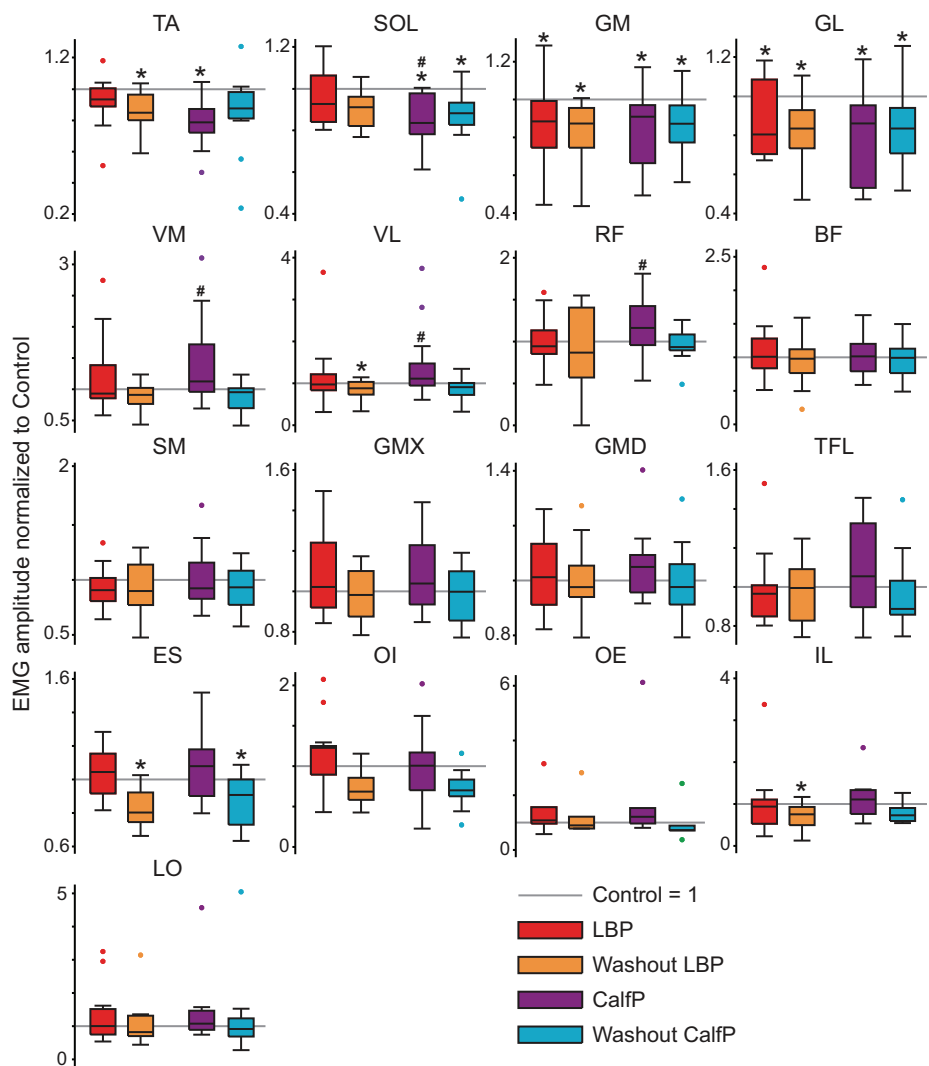


Fig. 4. Effect of experimental pain on muscle activity level. Myoelectric activity amplitude, normalized to the control condition [horizontal gray line (=1)], is shown with box plots for each muscle and each condition. Error bars, 95% CI; box, 25th to 75th percentile with the median. *Significant ($P < 0.05$) difference from control. #Significant ($P < 0.05$) difference between LBP and CalfP.

two pain locations in six participants (37.5%). VAF decreased by $>6.1\%$ in five participants (31.3%) during one of the two pain locations (four for LBP and one for CalfP, respectively; Fig. 7). Finally, five participants (31.3%) exhibited a decrease in VAF by $>6.1\%$ for both pain locations. When the EMG data of the CalfP condition were reconstructed with the synergy vectors of the LBP condition, these participants did not decrease VAF $>6.1\%$. This suggests the adaptation of muscle synergies between the two pain locations was similar in these five participants. Overall, muscle synergies were differently affected by pain locations in only 5 out of 16 participants.

Similarity of muscle synergies between experimental and control conditions. Synergies extracted for each condition independently were correlated to the control condition. Results from both synergy vectors and activations indicate that the synergy related to propulsion (*synergy 1*) and weight acceptance (*synergy 5*) were robust. In contrast, synergy related to leg deceleration (*synergy 2*), trunk extension (*synergy 4*) and especially trunk flexion (*synergy 3*) were more dependent on the experimental conditions, albeit not in all participants. From the 64 pairwise comparisons of the muscle synergy vectors between control and the other conditions, 6 (9%), 29 (45%), 31 (48%), 20 (31%), and 8 (13%) of the r -values were below threshold (0.80) for *synergies 1–5*, respectively (Fig. 8). For

the synergy activations coefficients, 1 (2%), 18 (28%), 41 (64%), 16 (25%), 4 (6%) of the r -values were below the threshold (0.80) for *synergies 1–5*, respectively (Fig. 8). Interestingly, timing of the peak activation of the synergy related to propulsion (*synergy 1*) was significantly affected by condition ($P < 0.01$). That is, the peak occurred earlier during CalfP than both during control (-6.4% of the gait cycle; $P < 0.01$) and LBP (-4.2% of the gait cycle; $P = 0.01$).

Similarity of muscle synergies between pain locations. Muscle synergies related to trunk flexion (*synergy 3*) and, to a lesser extent to trunk extension (*synergy 4*), were sensitive to pain location in some but not all participants. From the 16 pairwise comparison of the muscle synergy vectors between pain conditions, 3 (19%), 4 (25%), 10 (63%), 8 (50%), and 2 (13%) of the r -values were below threshold (0.80) for *synergies 1–5*, respectively (see Fig. 8). For the synergy activations coefficients, 1 (6%), 1 (6%), 11 (69%), 4 (25%), 1 (6%) of the r -values were below threshold (0.80) for *synergies 1–5*, respectively (Fig. 8).

DISCUSSION

The primary aim of this study was to examine how experimentally induced acute muscle pain affects motor control

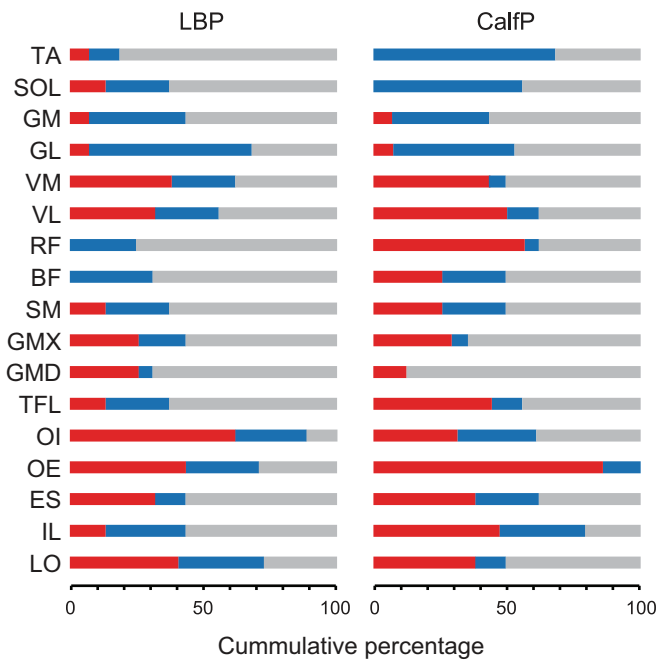


Fig. 5. Interindividual variability of change in EMG amplitude. The percentages of participants with increased (red), decreased (blue) and no change (gray) in muscle activation during LBP and CalfP relative to that in the control (>15% change) condition are displayed.

during gait with consideration of both muscle synergies and amplitude of muscle activity. The second aim was to examine potential differences in the effect of pain on motor control when it was induced in a low back or calf muscle. Overall, muscle synergies were altered very little in some participants ($n = 7$ for LBP and $n = 10$ for CalfP), but were more affected in the others ($n = 9$ for LBP and $n = 6$ for CalfP). A subgroup

Table 3. Description of muscle synergies

Synergy No.	Function	Timing	Major Muscle Contributions
1	Propulsion	Mid-late stance	Triceps surae
2	Leg deceleration	Late swing/early stance	Hamstrings
3	Trunk flexion	Swing/throughout the gait cycle	Abdominal muscles
4	Trunk extension	Late stance	Trunk extensors
5	Weight acceptance	Early stance	Quadriceps/gluteal muscles

of five participants showed similar changes between pain locations. Considering the whole group, most changes were observed in synergy related to trunk flexion (*synergy 3*) and to a lesser extent in synergy related to leg deceleration (*synergy 2*) and trunk extension (*synergy 4*). Both synergies related to propulsion (*synergy 1*) and weight acceptance (*synergy 5*) remained robust in most participants. Considering the amplitude of myoelectric activity, gastrocnemii activity was reduced during both pain conditions compared with control. Some lower leg muscles exhibited specific adaptations, depending on pain location (reduced SOL activity and increased VL and RF activity during CalfP compared with LBP).

Before considering the effect of pain, it is important to note that, although experimental (Berger et al. 2013; Overduin et al. 2012) and simulation data (Berniker et al. 2009; Neptune et al. 2009) support the hypothesis that the CNS produces movement through the flexible combination of muscle synergies, some authors suggest synergies simply reflect the underlying mechanical constraints (Kutch et al. 2008; Valero-Cuevas et al. 2009). Regardless of whether muscle synergies reflect “units of control” or task constraints, they provide a useful method to study the underlying

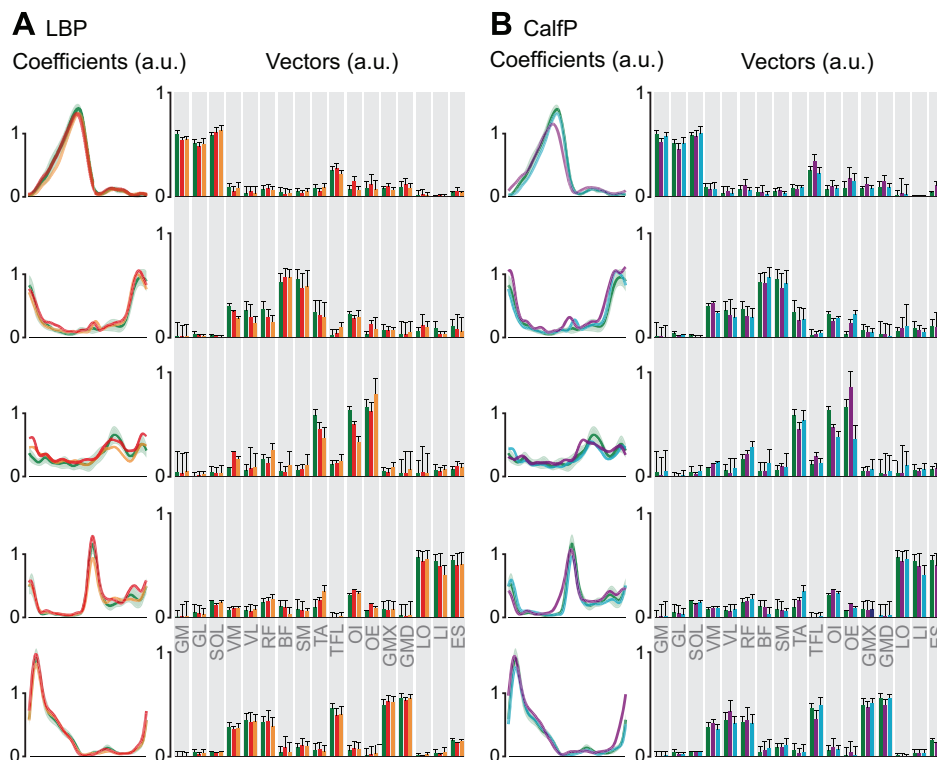


Fig. 6. Extracted muscle synergies for each condition. A: muscle synergy coefficients and vectors for control [green, with shaded green representing 95% CIs ($1.96 \times \text{SEM}$)], LBP (red) and washout LBP (orange). B: muscle synergy coefficients and vectors for control [green, with shaded green representing 95% CIs ($1.96 \times \text{SEM}$)], CalfP (purple) and washout CalfP (blue). Error bars, 95% CIs ($1.96 \times \text{SEM}$). a.u., Arbitrary units.

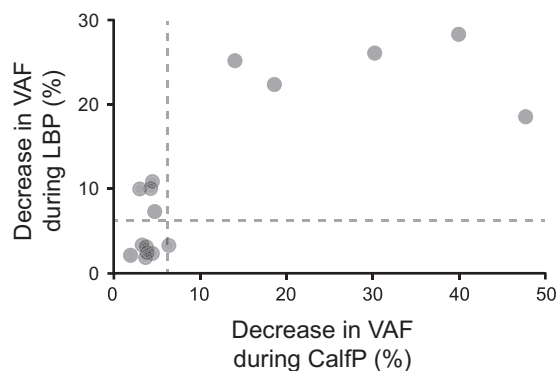


Fig. 7. Reduction in variance accounted for (VAF). Reduction in VAF when muscle patterns were reconstructed with muscle synergy vectors of the *control 1* condition compared with the VAF obtained when muscle patterns were reconstructed when muscle synergy vectors were allowed to vary in each pain conditions. The dashed gray lines represent the threshold of reduction (6.1%). This threshold was the upper limit of the 95% CI of the VAF change when EMG patterns of *control 2* were reconstructed using synergy vectors of *control 1*.

ing structure of muscle coordination from large EMG data sets (Safavynia et al. 2011).

The number of muscle synergies can reflect the complexity of motor control (Clark et al. 2010). In our experiment, five muscle synergies were extracted for each condition. Although the VAF by five synergies increased significantly during the two pain conditions, this increase was small (i.e., <2.6% of VAF). A synergy is classically considered relevant if its VAF exceeds 3–5% (Cappellini et al. 2006; Clark et al. 2010). Consequently, our results suggest that the complexity of motor control was not largely affected by experimental acute pain. However, the observation of a small change in VAF may be relevant and might imply a somewhat stricter neural control of movement.

Synergies related to propulsion (*synergy 1*) and weight acceptance (*synergy 5*) were mostly unaffected by pain. The robustness of these two synergies can be explained by the fact that they are the major power producer synergies (Allen and Neptune 2012) and are therefore important to maintain walking speed. Both the composition and the activation of synergies related to leg deceleration and trunk flexion/extension were more affected by experimental pain (Fig. 8), and this was more evident for some participants. The changes to trunk flexion/extension synergies are likely to be related to the changes observed in spine kinematics during both pain conditions. When pain was induced in the right lumbar ES muscle, participants may have adopted a protective strategy by avoiding movement toward the painful muscle. However, there was no systematic change in trunk muscle activity levels. Rather, a high intersubject variability in both changes in amplitude of trunk muscles activity (Fig. 5) and the composition of the synergy related to trunk flexion (*synergy 3*) was observed. This is in line with previous experiments that have shown that experimental LBP leads to a systematic increase in trunk stiffness in a group of healthy participants, but that the pattern of muscle activity to achieve this goal involved an individual-specific pattern of adaptation in muscle activity (Hodges et al. 2013). Overall, these trunk flexion/extension synergies are likely to be more adaptable during pain with high between-participants variability. The ability to adapt trunk muscle

synergies during gait was found earlier by Cappellini et al. (2006), who observed that, although synergies of lower leg muscles were robust between walking and running, synergies related to trunk muscles adapted to changing task constraints.

A basic assumption underpinning our understanding of the adaptation to movement during pain is that the primary aim of altered movement control is to modify the load on painful tissue to protect from further pain and/or injury (Hodges and Tucker 2011; Lund et al. 1991; van Dieën et al. 2003). Considering the redundancy of the musculoskeletal system, protection of the painful muscle (GM) during CalfP could have been achieved by profound changes in the propulsion synergy (*synergy 1*). Instead, composition of this synergy was largely unaltered. Furthermore, the amplitude of EMG of the whole triceps surae was reduced, as also partially reflected by the reduction of the propulsion synergy coefficient of activation.

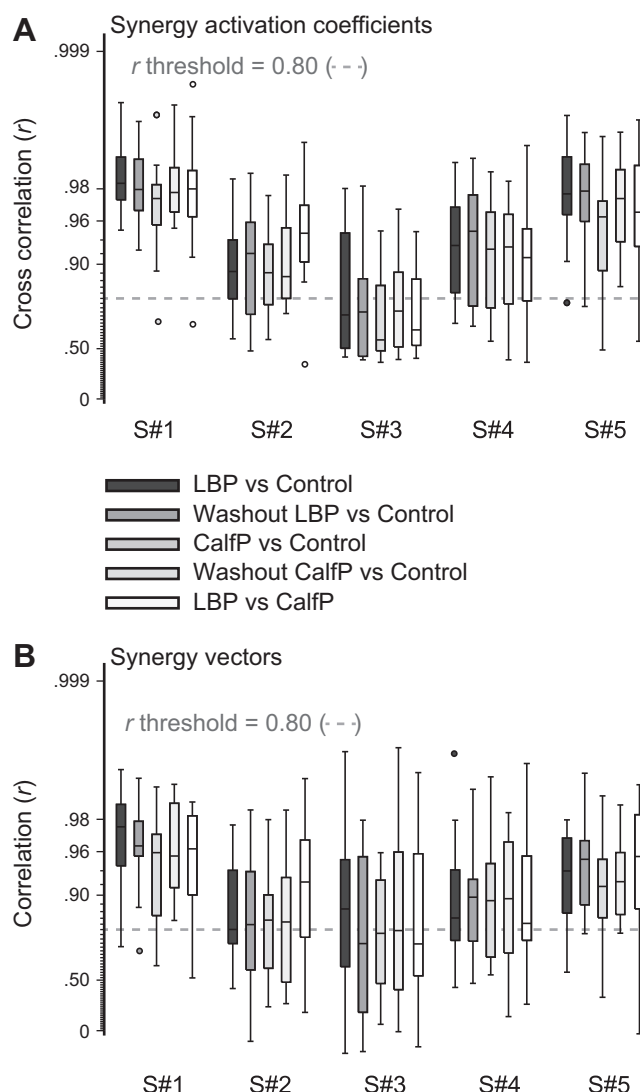


Fig. 8. Similarity of the muscle synergies compared with control. A: maximum Pearson cross-correlation coefficients (r) of the muscle synergy activation coefficients between control and LBP, washout LBP, CalfP, washout CalfP, and between LBP and CalfP. B: Pearson correlation coefficients (r) of the muscle synergy vector between control and LBP, washout LBP, CalfP, washout CalfP, and between LBP and CalfP. Data are depicted as median (line) (box, 25th to 75th percentile; error bars, 95% CI). Dashed light gray lines represent the thresholds set a priori. Note the scale is Fisher transformed.

The absence of systematic and selective inhibition of the painful muscle (i.e., medial gastrocnemius) could be explained by the fact that modification of muscle synergies would increase the complexity of control of the movement (higher cost for CNS as a result of an increase in the number of degrees of freedom to control). This is in line with a recent study that showed when force production capacity of one agonist muscles was reduced, participants simply increased the recruitment of all agonists, instead of recruiting only the nonaffected muscles (de Rugy et al. 2012). This suggests the selected pattern of muscle coordination is more “habitual” than “optimal”, as has been suggested by de Rugy et al. (2012). Several alternate explanations for the limited adaptation of the compositions of muscle synergies require consideration. First, muscle synergies (composition) might require a longer period to adapt than that provided by the transient exposure to noxious input used here. Second, mechanical interaction between the triceps surae muscles (Maas and Sandercock 2008) may limit the benefit of selective decrease in GM activity. Third, motor patterns can adapt independently between legs during gait (Choi and Bastian 2007), and the CNS might choose to compensate with the contralateral nonpainful leg rather than modify muscle synergies. Consistent with this proposal, kinematic data suggest that the participants adopted a limping strategy (and thus a compensation with the contralateral leg) during CalFP. Finally, it is important to consider the results of the present study in regards to the controlled speed imposed by the treadmill. Further investigations are necessary to determine whether motor adaptations are different during overground walking.

Although the synergy related to propulsion (*synergy 1*) remained largely unaltered with CalFP, the decrease in amplitude of the synergy activation coefficient coincided with decreased stride time. With a decrease in stride time (related to stride length during treadmill walking), less power is necessary for push off (Winter and Yack 1987). Although there might be a relation between reduced stride time and reduced activity of the triceps surae muscles during pain, stride time was not significantly different from control during the washout conditions, but triceps surae activity was still reduced in the washout condition. This limits simple interpretation of the interaction between EMG and kinematic changes. Although reduced activity of the entire triceps surae group may achieve the goal to reduce stresses within the painful muscle, it would require compensation in muscle activity between joints to maintain gait speed in spite of the decrease in stride time (Donelan et al. 2002a, 2002b). Moreover, ankle plantar flexion was reduced during CalFP, which could be a strategy to avoid large shortening and/or lengthening of the painful muscle.

Although hypertonic saline was injected into the ES at L₃, we did not observe any systematic change in amplitude in either the ES (L₃), IL or LO across participants. Rather, ES EMG significantly decreased during washout. Although this might be explained by a recent observation of latent intracortical inhibition after cessation of experimental pain (Schabrun et al. 2013), the alternate explanation is that this reduction was related to a more global difference in gait strategy (e.g., between leg coordination) during the washout.

Consistent with recent data (Hodges et al. 2013), substantial changes in EMG amplitude were identified for a number of muscles when data are considered for individual participants, but the pattern varied between them. Such interparticipant

variation could be expected in a highly redundant system and is in line with a proposed theory of adaptation to pain (Hodges and Tucker 2011). Interestingly, with LBP, many individuals increased activity of OI, OE and LO and could be interpreted as a solution to “brace” the trunk. In contrast, with CalFP a common adaptation was a decreased activity of the calf muscles. This could potentially highlight that the CNS adopts different solutions to “protect” the painful part with consideration of multiple factors and resolves to a different solution for different body parts and or function. These theories suggest complex adaptations that take into account redundancy, i.e., various solutions and previous experiences to adapt to pain.

To conclude, synergies related to propulsion (*synergy 1*) and weight acceptance (*synergy 5*) of the gait cycle were largely unaffected by acute nociceptor stimulation in a muscle that is either directly (GM) or indirectly related to gait (ES). In contrast, synergies related to the trunk flexion/extension and leg deceleration of gait could be altered with experimental pain in both locations, but more so for a subset of individuals. Further investigations are necessary to: 1) determine whether muscle coordination is affected differently in people with chronic pain; and 2) to better understand the individual variation, as it may explain why some people are more likely to develop persistence of a painful condition.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: W.v.d.H., P.W.H., J.H.v.D., and F.H. conception and design of research; W.v.d.H. and F.H. performed experiments; W.v.d.H. and F.H. analyzed data; W.v.d.H., P.W.H., J.H.v.D., and F.H. interpreted results of experiments; W.v.d.H. prepared figures; W.v.d.H., P.W.H., J.H.v.D., and F.H. drafted manuscript; W.v.d.H., P.W.H., J.H.v.D., and F.H. edited and revised manuscript; W.v.d.H., P.W.H., J.H.v.D., and F.H. approved final version of manuscript.

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